PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Mark Brader, *et al.*	
Serial No.: 08/484,542	
Filed: June 7, 1995	Group Art Unit: 1631
For: **Stabilized, Acylated Insulin Formulations**	Examiner: M. Allen
Docket No.: X-10097	

DECLARATION OF MR. MICHAEL ROY UNDER 37 C.F.R. § 1.608(b)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Michael L. Roy declares as follows.

1. I received a B.S. in Chemistry from Kansas State University in 1966 and a M.S. in Physical Chemistry from Purdue University in 1974. I have worked in the field of freeze-drying pharmaceuticals for about 25 years. I have been employed by Eli Lilly & Company as a pharmaceutical chemist for the past 33 years.

2. I am not a co-inventor in the above-referenced patent application. The work I discuss in this declaration relates to freeze-dried samples I prepared from several solutions received from Dr. Mark Brader on or about September 9, 1993.

3. Exhibit 3 is a photocopy of a chart tracing obtained during a freeze-drying procedure for four samples received from Dr. Mark Brader. I recognize this Exhibit as a photocopy of a chart tracing I generated. I confirm the notes on the chart tracing are in my handwriting. The original chart tracing was printed on September 9, 1993, as indicated by my notation of the date in the bottom right of the tracing. It is my custom to write the run number in terms of the date on which the freeze-drying procedure begins on each chart tracing I generate. Thus, the P090993 run number on the first page of the chart tracing indicates that I started the freeze-drying run on September 9, 1993. The chart tracing also indicates that I freeze-dried four different samples which were labeled BGX203, DBF40, DBF40Zn, and DXG209.

4. The above-referenced samples were processed according to the procedure I generally use before freeze drying. The samples were filtered through a 0.45 micron filter and 1 ml aliquots were transferred into 5 ml vials. Thus, for each sample, about 10 vials containing 1 ml of filtered sample were freeze dried.

5. Vials were loaded into a Virtis 25 SRCX freeze-dryer. The freeze-dryer was set to an initial temperature lower than $-35^{0}C$ to freeze the samples. After 2 hours and 15 minutes, the temperature was set at $-10^{0}C$ and the samples were subjected to a reduced pressure of 120 microns of mercury absolute. The samples were dried over night. The chart tracing indicates all the ice was removed after approximately 9 hours. The next day the samples were subject to secondary drying which removed any bound water that was not removed as ice. For secondary drying, the temperature was increased to $30^{0}C$ for 3.5 hours.

6. Following secondary drying on September 10, 1993, the vials were sealed. About forty sealed vials containing lyophilized sample were transferred back to Dr. Mark Brader.

7. Line tracing labels as depicted on the chart submitted as Exhibit 3 are as follows:
Line 3 - sample temperature
Lines 10 & 11 - shelf temperature
Line 20 - chamber pressure
Line 21 - vapor pressure in chamber
Line 23 - chart zero.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information of belief are believed to be true; and I am warned that all statements made herein were made with the knowledge that willful false statements are punishment by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful and false statements may jeopardize the validity of any patent issued from this application.

Michael L Roy

Michael L. Roy

April 23, 2003

Date